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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/807,599 | 04/13/2001 | Yuji Ishihara | 2566US0P | 9278 |

23115 7590 03/26/2003

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT PAPER NUMBER

1624

DATE MAILED: 03/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/807,599

Applicant(s)
ISHIHARA et al.

Examiner
Brenda Coleman

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 14, 2003
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-15, 17, 22, 43, and 44 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-5, 7-11, 14, 15, 22, 43, and 44 is/are allowed.
- 6) ☒ Claim(s) 12, 13, and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

Claims 1-5, 7-15, 17, 22, 43 and 44 are pending in the application.

This action is in response to applicants' amendment filed January 14, 2003. Claims 6, 16, 18-21 and 23-42 have been canceled and claims 1, 12, 15 and 17 have been amended.

Response to Amendment

Applicant's amendments filed January 14, 2003 have been fully considered with the following effect:

1. The applicant's amendments are sufficient to overcome the improper Markush rejection of claims 1-3, 7-15, 17-23, 43 and 44 of the last office action, which is hereby **withdrawn**.
2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claim 13 of the last office action, applicants' stated that "Pro-drugs are defined in detail in the specification at page 40, line 12 - page 41, line 15". However, the definition of prodrug in the specification is such that a "prodrug of Compound (I) refers to a compound which is converted into Compound (I) by the action of an enzyme or gastric juice and the like under physiological conditions in vivo".

The term prodrug is of indeterminate scope in that they vary widely from drug to drug. It is not known which moiety of formula I would form the basis for the prodrug. Every ester, amide and carbamate in theory is biohydrolyzable, i.e. is capable in some degree of hydrolyses. Not to mention the many in vivo environments that this occurs in.

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The applicants' further stated that "there is guidance in the specification detailing which modifications may be made at which portions of the molecule to provide the recited pro-drugs". The specification states that "examples of prodrugs of compound (I) include compounds derived by acylation, alkylation or phosphorylation of the amino group", "compounds derived by acylation, alkylation, phosphorylation or boration of the hydroxy group", "compounds derived by esterification or amidation of the carboxyl group". The compounds of formula (I) possess more than one amino group and may possess more than one carboxyl group or hydroxy group.

It is the *Wands* factors which are used to evaluate the enablement question. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace substituted benzazepine compounds. The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claims 13 and 17. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

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Claims 13 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For reasons of record and stated above.

3. The applicant's amendments are sufficient to overcome the 35 USC § 112, second paragraph rejections of the last office action, which are hereby **withdrawn**.

In view of the amendment dated January 14, 2003, the following new grounds of rejection apply:

Specification

4. The disclosure is objected to because of the following informalities: the amendment to paragraph 4 on page 28 contains two typographical errors, i.e. **terahydro**-1H-1-benzazepine and **terahydro**-1H-2-benzazepine. See line 5 of the amendment.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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5. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The second species on page 28 is not described in the specification with respect to the compounds of formula (I), i.e. 2-(phenylmethyl)-8-[2-[1-[[4-(N,N-diethylaminomethyl)phenyl]methyl]-4-piperidinyl]ethoxy]-2,3,4,5-tetrahydro-1H-2-benzazepine. The [4-(N,N-diethylaminomethyl)phenyl]methyl portion of the molecule corresponds to the R¹ substituent of formula (I) where R¹ is a hydrocarbon group optionally having a substituent. However, the substituent of the 2nd species on page 28 is not described in the specification with respect to the substituents on the hydrocarbon where the hydrocarbon is phenylmethyl and the substituent is a diethylamino substituted alkyl, i.e. diethylaminomethyl.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claim 12 is vague and indefinite in that it is not known what is meant by the third species which is missing an close parenthesis and an open bracket, i.e. 3-[1-

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(phenylmethyl]-4-piperidinyl]-1-[3-(phenylmethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-7-y;]-1-propanone oxime.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 12 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The species where R¹ is [4-(N,N-diethylaminomethyl)phenyl]methyl does not fall within the genus, thus there is no statement of utility for this species and credibility will not be assessed.

Allowable Subject Matter

8. Claims 1-5, 7-11, 14, 15, 22, 43 and 44 allowed. None of the prior art of record nor a search in the pertinent art area teaches the compounds, method of use or process of preparing the compounds of formula (I) as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays and Tuesdays from 9:00 AM to 3:00 PM and from 5:30 PM to 7:30 PM and on Wednesday thru Friday from 9:00 AM to 6:00 PM.

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The fax phone number for this Group is (703) 308-4734 for “unofficial” purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.



Brenda Coleman
Primary Examiner AU 1624
March 21, 2003